PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)*	03 SEP 1996
Applicant's or agent's file reference: 06519/002WO1	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/US95/06742	26 MAY 1995	27 MAY 1994

Applicant
UNIVERSITY OF COLORADO

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	BRUCE CAMPELL
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/IPEA/416 (July 1992)★

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 06519/002WO1	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US95/06742	International filing date *(day/month/year)* 26 MAY 1995	Priority date *(day/month/year)* 27 MAY 1994
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant UNIVERSITY OF COLORADO		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15 DECEMBER 1995	19 AUGUST 1996
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer BRUCE CAMPELL Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (January 1994)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US95/06742

I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments)*:

[X] the international application as originally filed.

[X] the description, pages 1-40 , as originally filed.
pages NONE , filed with the demand.
pages NONE , filed with the letter of _____.
pages _____ , filed with the letter of _____.

[X] the claims, Nos. 1-21 , as originally filed.
Nos. NONE , as amended under Article 19.
Nos. NONE , filed with the demand.
Nos. NONE , filed with the letter of _____.
Nos. _____ , filed with the letter of _____.

[X] the drawings, sheets/~~fig~~ 1-2 , as originally filed.
sheets/~~fig~~ NONE , filed with the demand.
sheets/~~fig~~ NONE , filed with the letter of _____.
sheets/~~fig~~ _____ , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

[X] the description, pages NONE.

[X] the claims, Nos. NONE.

[X] the drawings, sheets/~~fig~~ NONE.

3. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US95/06742

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	1-11, 13-21	YES
	Claims	12	NO
Inventive Step (IS)	Claims	2-5, 21	YES
	Claims	1, 6-20	NO
Industrial Applicability (IA)	Claims	1-20	YES
	Claims	21	NO

2. CITATIONS AND EXPLANATIONS

Claim 12 lacks novelty under PCT Article 33(2) as being anticipated by Selawry et al. Selawry et al. disclose a method for suppressing rejection of islet cells by also administering Sertoli cells, which express Fas ligand.

Claims 1, 6, 7, 10, 11 and 13-20 lack an inventive step under PCT Article 33(3) as being obvious over Takahashi et al (Cell, 1994). Takahashi et al. disclose the sequence of the mouse Fas ligand (Figure 1). Takahashi et al. teach that the Fas ligand induces apoptosis in Fas-expressing cells (page 972, column 2). Takahashi et al. teach that activated T cells express Fas, and suggest that Fas ligand is involved in induction of peripheral tolerance (page 973). Takahashi et al. do not teach pharmaceutical compositions or clinical methods.
It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a pharmaceutical composition comprising the mouse Fas ligand. One would have been motivated to do so, given the known effect of Fas ligand in causing apoptosis in mature activated T cells. There would have been a reasonable expectation that so killing activated T cells would have suppressed T cell mediated phenomena, such as graft rejection, T cell mediated disease or disease recurrence, and inflammation. Similarly, it would have been obvious that detection of Fas ligand would be useful in selecting suitable graft donor tissue or graft recipient sites. Thus the invention as a whole was *prima facie* obvious to one of ordinary skill in the art.

Claims 8 and 9 lack an inventive step under PCT Article 33(3) as being obvious over Takahashi et al (Cell, 1994) in view of Johnstone et al and Lee et al. Takahashi et al disclose the mouse Fas ligand, as discussed above. Takahashi et al. do not disclose antibodies against the Fas ligand. Johnstone et al teach methods for producing antibodies. Lee et al teach a method for determining what cell types express Fas, utilizing an antibody against Fas.
It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the methods of Johnstone (Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(6): A01N 37/18, 63/00; A61K 38/00; C07H 21/04; C07K 1/00, 16/00; C12N 15/00 and US Cl.: 424/93.1, 93.2, 93.21; 435/172.3, 320.1; 514/2; 530/350, 387.1; 536/23.5, 23.51

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
et al. to produce antibodies against the Fas ligand disclosed by Takahashi et al. One would have been motivated to do so in order to study expression of the Fas ligand in a manner analogous to that used by Lee et al. Thus the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 21 lacks industrial applicability as defined by PCT Article 33(4). Immune "protection" is provided by the Fas ligand protein, not the DNA encoding it. Therefore, in the event that a gene or a viral vector were attacked by activated host T cells, it is not expected that physical attachment of the DNA sequence would provide any protection.

Claims 1 and 6-20 meet the criteria set out in PCT Article 33(4).

Claims 1, 6-11 and 13-21 meet the criteria set out in PCT Article 33(2).

Claims 2-5 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the sequence of the human Fas ligand.

---------- NEW CITATIONS ----------
SELAWRY et al. Sertoli cell-enriched fractions in successful islet cell transplantation. Cell Transplantation. 1993, Vol. 2, pages 123-129, see the entire document.